



Rabson-Mendenhall syndrome

Rabson-Mendenhall syndrome is a rare disorder characterized by severe insulin resistance, a condition in which the body's tissues and organs do not respond properly to the hormone insulin. Insulin normally helps regulate blood sugar levels by controlling how much sugar (in the form of glucose) is passed from the bloodstream into cells to be used as energy. In people with Rabson-Mendenhall syndrome, insulin resistance impairs blood sugar regulation and ultimately leads to a condition called diabetes mellitus, in which blood sugar levels can become dangerously high.

Severe insulin resistance in people with Rabson-Mendenhall syndrome affects the development of many parts of the body. Affected individuals are unusually small starting before birth, and infants experience failure to thrive, which means they do not grow and gain weight at the expected rate. Additional features of the condition that become apparent early in life include a lack of fatty tissue under the skin (subcutaneous fat); wasting (atrophy) of muscles; dental abnormalities; excessive body hair growth (hirsutism); multiple cysts on the ovaries in females; and enlargement of the nipples, genitalia, kidneys, heart, and other organs. Most affected individuals also have a skin condition called acanthosis nigricans, in which the skin in body folds and creases becomes thick, dark, and velvety. Distinctive facial features in people with Rabson-Mendenhall syndrome include prominent, widely spaced eyes; a broad nose; and large, low-set ears.

Rabson-Mendenhall syndrome is one of a group of related conditions described as inherited severe insulin resistance syndromes. These disorders, which also include Donohue syndrome and type A insulin resistance syndrome, are considered part of a spectrum. Rabson-Mendenhall syndrome is intermediate in severity between Donohue syndrome (which is usually fatal before age 2) and type A insulin resistance syndrome (which is often not diagnosed until adolescence). People with Rabson-Mendenhall syndrome develop signs and symptoms early in life and live into their teens or twenties. Death usually results from complications related to diabetes mellitus, such as a toxic buildup of acids called ketones in the body (diabetic ketoacidosis).

Frequency

Rabson-Mendenhall syndrome is estimated to affect less than 1 per million people worldwide. Several dozen cases have been reported in the medical literature.

Genetic Changes

Rabson-Mendenhall syndrome results from mutations in the *INSR* gene. This gene provides instructions for making a protein called an insulin receptor, which is found

in many types of cells. Insulin receptors are embedded in the outer membrane surrounding the cell, where they attach (bind) to insulin circulating in the bloodstream. This binding triggers signaling pathways that influence many cell functions.

The *INSR* gene mutations that cause Rabson-Mendenhall syndrome reduce the number of insulin receptors that reach the cell membrane or diminish the function of these receptors. Although insulin is present in the bloodstream, without enough functional receptors it is less able to exert its effects on cells and tissues. This severe resistance to the effects of insulin impairs blood sugar regulation and affects many aspects of development in people with Rabson-Mendenhall syndrome.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Mendenhall syndrome
- pineal hyperplasia and diabetes mellitus syndrome
- pineal hyperplasia, insulin-resistant diabetes mellitus, and somatic abnormalities
- RMS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Pineal hyperplasia AND diabetes mellitus syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0271695/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Acanthosis Nigricans
<https://medlineplus.gov/ency/article/000852.htm>
- Encyclopedia: Diabetic Ketoacidosis
<https://medlineplus.gov/ency/article/000320.htm>
- Encyclopedia: Failure to Thrive
<https://medlineplus.gov/ency/article/000991.htm>
- Encyclopedia: Ovarian Cysts
<https://medlineplus.gov/ency/article/001504.htm>
- Health Topic: Blood Sugar
<https://medlineplus.gov/bloodsugar.html>
- Health Topic: Diabetes
<https://medlineplus.gov/diabetes.html>

Genetic and Rare Diseases Information Center

- Rabson-Mendenhall syndrome
<https://rarediseases.info.nih.gov/diseases/226/rabson-mendenhall-syndrome>

Additional NIH Resources

- National Institute of Diabetes and Digestive and Kidney Diseases: Insulin Resistance and Prediabetes
<https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes/prediabetes-insulin-resistance>
- National Institute of Diabetes and Digestive and Kidney Diseases: Your Guide to Diabetes: Type 1 and Type 2
<https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes>

Educational Resources

- Cambridge University Hospitals (UK): What is Severe Insulin Resistance?
<http://www.cuh.org.uk/addenbrookes-hospital/services/national-severe-insulin-resistance-service/national-severe-insulin-resistance-service/what-severe-insulin-resistance>
- Disease InfoSearch: Pineal hyperplasia AND diabetes mellitus syndrome
<http://www.diseaseinfosearch.org/Pineal+hyperplasia+AND+diabetes+mellitus+syndrome/9115>
- MalaCards: rabson-mendenhall syndrome
http://www.malacards.org/card/rabson_mendenhall_syndrome

- Merck Manual Consumer Version: Diabetes Mellitus
<http://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/diabetes-mellitus-dm-and-disorders-of-blood-sugar-metabolism/diabetes-mellitus-dm>
- Orphanet: Rabson-Mendenhall syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=769

Patient Support and Advocacy Resources

- American Diabetes Association
<http://www.diabetes.org/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/rabson-mendenhall-syndrome/>
- Resource List from the University of Kansas Medical Center: Diabetes
<http://www.kumc.edu/gec/support/diabetes.html>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Rabson-Mendenhall+syndrome%22+OR+%22Mendenhall+syndrome%22+OR+%22pineal+hyperplasia+and+diabetes+mellitus+syndrome%22+OR+%22pineal+hyperplasia%2C+insulin-resistant+diabetes+mellitus%2C+and+somatic+abnormalities%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28Rabson-Mendenhall+syndrome%5BTIAB%5D%29+OR+%28Mendenhall+syndrome%5BTIAB%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- PINEAL HYPERPLASIA, INSULIN-RESISTANT DIABETES MELLITUS, AND SOMATIC ABNORMALITIES
<http://omim.org/entry/262190>

Sources for This Summary

- Grasso V, Colombo C, Favalli V, Galderisi A, Rabbone I, Gombos S, Bonora E, Massa O, Meschi F, Cerutti F, Iafusco D, Bonfanti R, Monciotti C, Barbetti F. Six cases with severe insulin resistance (SIR) associated with mutations of insulin receptor: Is a Bartter-like syndrome a feature of congenital SIR? *Acta Diabetol.* 2013 Dec;50(6):951-7. doi: 10.1007/s00592-013-0490-x. Epub 2013 Jul 4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23824322>
- Jiang S, Fang Q, Zhang F, Wan H, Zhang R, Wang C, Bao Y, Zhang L, Ma X, Lu J, Gao F, Xiang K, Jia W. Functional characterization of insulin receptor gene mutations contributing to Rabson-Mendenhall syndrome - phenotypic heterogeneity of insulin receptor gene mutations. *Endocr J.* 2011;58(11):931-40. Epub 2011 Aug 23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21869538>
- Longo N, Wang Y, Smith SA, Langley SD, DiMeglio LA, Giannella-Neto D. Genotype-phenotype correlation in inherited severe insulin resistance. *Hum Mol Genet.* 2002 Jun 1;11(12):1465-75.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12023989>
- Musso C, Cochran E, Moran SA, Skarulis MC, Oral EA, Taylor S, Gorden P. Clinical course of genetic diseases of the insulin receptor (type A and Rabson-Mendenhall syndromes): a 30-year prospective. *Medicine (Baltimore).* 2004 Jul;83(4):209-22. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15232309>
- Parker VE, Semple RK. Genetics in endocrinology: genetic forms of severe insulin resistance: what endocrinologists should know. *Eur J Endocrinol.* 2013 Sep 12;169(4):R71-80. doi: 10.1530/EJE-13-0327. Print 2013 Oct. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23857978>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4359904/>
- Semple RK, Savage DB, Cochran EK, Gorden P, O'Rahilly S. Genetic syndromes of severe insulin resistance. *Endocr Rev.* 2011 Aug;32(4):498-514. doi: 10.1210/er.2010-0020. Epub 2011 May 2. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21536711>

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/rabson-mendenhall-syndrome>

Reviewed: December 2014

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services